

WE CLAIM:

1. An amino acid sequence comprising antithrombin having an H-helix, wherein at least one amino acid of the H-helix is modified to have a more positive charge than an H-helix of non-modified antithrombin.
2. The amino acid sequence of claim 1, wherein at least one negatively charged amino acid of the non-modified H-helix is substituted with a neutral or positively charged amino acid to form the modified H-helix.
3. The amino acid sequence of claim 1, wherein at least one neutral amino acid of the non-modified H-helix is substituted with a positively-charged amino acid to form the modified H-helix.
4. A modified antithrombin protein having one or more amino acids in the region of amino acids 304-314 modified to have a more positive charge than non-modified antithrombin.
5. A pharmaceutical composition comprising the modified antithrombin protein of claim 4.
6. The modified antithrombin protein of claim 4, having one or more of the following amino acid substitutions: D309K, E310K, E312K, E313K, D309R, E310R, E312R, E313R.
7. A pharmaceutical composition comprising the modified antithrombin protein of claim 6.
8. The modified antithrombin protein of claim 6, having the following amino acid substitutions: D309K, E310K, E312K, E313K.

9. A nucleic acid sequence encoding a modified antithrombin having at least one nucleic acid modified to encode at least one modified amino acid of the antithrombin H-helix, such that the H-helix has a more positive charge than a H-helix of non-modified antithrombin.
10. The nucleic acid sequence of claim 9, encoding a modified antithrombin protein having one or more amino acids in the region of amino acids 304-314 modified to carry a more positive charge than non-modified antithrombin.
11. The nucleic acid sequence of claim 10, wherein said one or more modified nucleic acid results in one or more of the following amino acid substitutions: D309K, E310K, E312K, E313K, D309R, E310R, E312R, E313R.
12. The nucleic acid sequence of claim 11, wherein said one or more modified nucleic acid results in one or more of the following amino acid substitutions: D309K, E310K, E312K, E313K.
13. A method for inhibiting the activity of thrombin bound to thrombomodulin (T-TM) in a patient, comprising administering to said patient an effective inhibitory amount of a modified antithrombin, wherein at least one amino acid of the antithrombin H-helix is modified to carry a more positive charge than a H-helix of non-modified antithrombin.
14. A method for inhibiting the activation of Protein C by thrombin bound to thrombomodulin (T-TM) in an animal, comprising contacting said T-TM with an effective inhibitory amount of a modified antithrombin, wherein at least one amino acid of the antithrombin H-helix is modified to carry a more positive charge than a H-helix of non-modified antithrombin.

15. A method for inhibiting Activated Protein C degradation of one or more of Coagulation Factors V, VIII, or X in an animal, comprising contacting said sample with an effective inhibitory amount of a modified antithrombin, wherein at least one amino acid of the antithrombin H-helix is modified to carry a more positive charge than a H-helix of non-modified antithrombin.
16. A method for treating coagulation deficiency in a patient comprising administering to said patient an effective procoagulant amount of a modified antithrombin, wherein at least one amino acid of the antithrombin H-helix is modified to carry a more positive charge than a H-helix of non-modified antithrombin.
17. The method of claim 16, wherein the modified antithrombin has one or more amino acids in the region of amino acids 304-314 modified to have a more positive charge than non-modified antithrombin.
18. The method of claim 17, wherein the modified antithrombin has one or more of the following amino acid substitutions: D309K, E310K, E312K, E313K, D309R, E310R, E312R, E313R.
19. A method for treating hemophilia comprising administering to a patient in need thereof an effective amount of the modified antithrombin of claim 4.
20. A method for extending the bioavailability of Factor VIII in a patient, comprising administering to the patient an effective amount of a modified antithrombin, wherein at least one amino acid of the antithrombin H-helix is modified to carry a more positive charge than a H-helix of non-modified antithrombin, and wherein said amount is effective to inhibit degradation of Factor VIII.

21. The method of claim 20, wherein the modified antithrombin has one or more amino acids in the region of amino acids 304-314 modified to have a more positive charge than non-modified antithrombin.

22. The method of claim 21, wherein the modified antithrombin has one or more of the following amino acid substitutions: D309K, E310K, E312K, E313K, D309R, E310R, E312R, E313R.

23. The pharmaceutical composition of claim 5, further comprising a therapeutically effective amount of Factor VIII.

24. The pharmaceutical composition of claim 23, comprising a molar ratio of approximately 1:1 of said AT-pos to Factor VIII .

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